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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,463	07/01/2003	Francisco Cruz	67-97A	3099

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EXAMINER
SOROUSH, LAYLA

ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/612,463	CRUZ ET AL.	
	Examiner	Art Unit	
	Layla Soroush	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed October 5, 2007 presents remarks and arguments submitted to the office action mailed April 5, 2007 is acknowledged.

Claims 1-3, 5-10 are pending.

Applicant's arguments over the Claim objection over Claim 3 is persuasive due to amendments made to the claim. Therefore, the rejection is herewith withdrawn.

Applicant's arguments over the 35 U.S.C. 102 (b) rejection of claims 1, 5, and 6-7 over Craft et al. (Temporal Parameters of Desensitization to Intravesical Resiniferatoxin in the Rat, Physiol. Behave. V ol. 56, No. 3, pp. 479-486, 1994 - IDS) is not persuasive. Therefore, the rejection of record is maintained.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 2 and 3 over Craft et al. (Temporal Parameters of Desensitization to Intravesical Resiniferatoxin in the Rat, Physiol. Behave. V ol. 56, No. 3, pp. 479-486, 1994 - IDS) in view of Blumberg (4,939,149 -- IDS)) is not persuasive. Therefore, the rejection of record is maintained.

Applicant's presented no arguments over the 35 U.S.C. 103 (a) rejection of claims 8-10 over Craft et al. (Temporal Parameters of Desensitization to Intravesical Resiniferatoxin in the Rat, Physiol. Behave. V ol. 56, No. 3, pp. 479-486, 1994 - IDS) in view Ebert US Pat No. 2,182,075). Therefore, the rejection of record is maintained.

Applicant's presented no arguments over the Obvious Double Patenting rejection of Patent Application No. 09/138,448 (US Pat No. 6630515). Therefore, the rejection is maintained for the reasons of record.

The rejections are restated below for applicant's convenience:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, and 6-7 rejected under 35 U.S.C. 102(b) as being anticipated by Craft et al. (Temporal Parameters of Desensitization to Intravesical Resiniferatoxin in the Rat, Physiol. Behave. Vol. 56, No. 3, pp. 479-486, 1994 - IDS).

Craft et al. teaches intravesicular instillation administration of resiniferatoxin at 0.33uM concentration. The resiniferatoxin was dissolved in

≤ 2 % ethanol to which 1% Tween-80 (nonoionic detergent) and saline were added (see page 480, Drugs). The concentration limitation is met by the teachings of the reference.

Further, the prior art reads on the limitation of a first and second container; because the compounds must necessarily be contained in containers, and the teaching that the resiniferatoxin was dissolved in ethanol and Tween-80 and saline were added supports the fact that there are separate containers, one holding the resiniferatoxin and the other diluents.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Craft et al. ((1)Temporal Parameters of Desensitization to Intravesical Resiniferatoxin in the Rat, Physiol. Behave. Vol. 56, No. 3, pp. 479-486, 1994 - IDS) in view of Blumberg (US Pat No 4,939,149).

Craft et al. is as discussed above.

Craft et al.(1) does not teach the specific concentration and the amounts of the components as recited in claims 2 and 3.

Blumberg teaches "The desirable dose of the compounds of the present invention varies with the subject, drug form, method and period of administration. However, in order to obtain desirable effects, generally it is recommended to administer 0.1.times.10.sup.-3 to 5.times.10.sup.-2 mg/kg, preferably 0.1.times.10.sup.-3 to 5.times.10.sup.-3 mg/kg, body weight of the compounds of the present invention for single application, or less upon multiple application. In terms of composition, compounds should be present between. 0.0001 to 10% by weight, preferably 0.0001 to 1% by weight." Based on the average weight of human (60 kg) the concentration of the active compound is preferably between 0.01-0.5 uM (column 5 lines 25-40).

The RTX compounds were administered in 10% ethanol, 10% Tween-80/ 80% physiological saline solution unless otherwise indicated (column 6, lines 5-16).

The active agent is either in a concentrate solution or lyophilized powder form.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to manipulate specific concentration and the amounts of the components parameters. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable

ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The motivation to change the amounts and concentration is because they are deemed to be manipulatable parameters practiced by an artisan to obtain the best possible pharmaceutical results.

Claims 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Craft et al. (Temporal Parameters of Desensitization to Intravesical Resiniferatoxin in the Rat, Physiol. Behave. Vol. 56, No. 3, pp. 479-486, 1994 - IDS) as applied to claims 1-3, 5-7, and further in view of Ebert (US Pat 2,182,075).

Craft et al. is as discussed above.

The reference does not teach buffering salts as recited in claims 8-10.

Ebert teaches buffering materials are used in a injectable composition to adjust the pH of their solution to about 7-7.4.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a buffering material. The motivation to make such an incorporation is because the reference teaches that injections are preferably adjusted in pH and said buffering material are used in compositions to adjust the pH of their solution to about 7-7.4. Additionally the reference teaches the buffering salts are used to avoid irritation. A skilled artisan would therefore, have reasonable expectation of producing a composition with a pH of about 7-7.4 to avoid irritation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7-9, 11, and 13 of U.S. Patent Application No. 09/138,448. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application recites A method for alleviating symptoms of neurogenic urinary dysfunction comprising administering by intravesicular instillation to a human patient having said symptoms a therapeutically effective concentration in the range from 0.05 uM to 2.0 mM of a compound selected from the group resiniferatoxin, tinyatoxin, 20-homovanillyl-mezerein or 20-

homovanillyl-12-deoxyphorbol-13-phenylacetate in a physiologically compatible solvent, said concentration being a concentration that does not cause meaningful burning or irritation to said patient, whereas the instant claims are A kit for intravesicular instillation comprising, a first container containing a unit dose of a therapeutic compound selected from the group resiniferatoxin, tinyatoxin, 20-homovanillyl-mezerein or 20-homovanillyl-12-deoxyphorbol-13-phenylacetate in a solution concentrate or dry powder form and a second container containing a physiologically compatible diluent capable of dissolving and maintaining in solution the therapeutic compound, the volume of said diluent being sufficient for intravesicular instillation of the unit dose and providing a concentration of the therapeutic compound of from 0.05 uM to 2.uM upon mixing the diluent with the therapeutic compound, and means for combining the diluent with the stock solution or lyophilized powder under sterile conditions. To one of ordinary skill in the art it would be obvious to employ an I.V. instillation kit herein containing a unit dosage of the active compound and solvent in which resiniferatoxin is to be dissolved is considered obvious since the active compound is known to be useful in injection compositions containing the same solvents.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed October 5, 2007 have been fully considered.

The response to the arguments is as discussed below:

Examiner has inadvertently quoted what was supposed to be a paraphrase of the prior art. The argument regarding the Craft reference is still not persuasive.

Applicant argues that the Examiner's calculation of RTX is incorrect.

Craft et al. teaches 0.3 mL of vehicle or RTX was injected into the bladder of treated rats (see p. 480 col. 1 lines 58-59). Figure 1 shows that 0 to 10.0 nmol of RTX was administered.

Molarity = moles of solute/ 1 L solution

For example, 0.1 nmoles was taught in Figure 1 -- to convert to uMol:

0.1 nmoles/ 0.3 mL = 0.1 nmoles / 3*10^-4 L = 333.3 nmoles / L =

0.333 umoles/ 1L = 0.333uM.

Applicant's arguments are not persuasive.

Applicant argues that Blumberg fails to disclose the claimed concentration range is not persuasive. It would be obvious to one of ordinary skill in the art to adjust the concentration of RTX in order to achieve a desirable effect in a subject of different body weight as taught by Blumberg. Although, Blumberg teaches that RTX should present in a composition between 0.0001 to 10%. One of ordinary skill is required for administration to a subject the amount of RTX in the composition can be adjusted to achieve the desired effects taught by Blumberg.

The arguments are not persuasive and the rejection is made **FINAL**.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed

within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-

direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER